Future Directions in the Use of Echocardiography

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SUMMARY The heart may play an active, passive, or incidental role in the pathogenesis of hypertension. Echocardiography probably contributes little to understanding of active mechanisms, although it may provide important information relative to structural and functional adaptive changes associated with development of left ventricular hypertrophy. Moreover, because other clinical conditions frequently coexist with hypertensive heart disease, echocardiography may provide another dimension in the assessment of obesity, coronary heart disease, mitral valve prolapse, idiopathic hypertrophic subaortic stenosis, and asymmetric septal hypertrophy in the overall problem. Critical in this understanding are the subtle changes that occur in the individual patient, reflecting the natural history of the disease or response to its treatment. Since technical problems preclude echocardiographic evaluation in all patients with hypertension, particular care must be exercised in making epidemiologic generalizations. (Hypertension 9 [Suppl II]: II-77-II-80, 1987)

KEY WORDS • hypertensive heart disease • left ventricular hypertrophy • regression of ventricular mass • antihypertensive therapy • asymmetric septal hypertrophy • mitral valve prolapse • idiopathic hypertrophic subaortic stenosis • epidemiology

Written above the National Archives Building in Washington, D.C., is the phrase, “What is past is prologue.” This epigram is pertinent to our discussion since before we can assess the future directions for the use of echocardiography in hypertension we must refer back to our past investigations and how they have influenced our thinking on the role of the heart in hypertension.

The Heart in Hypertension

The heart may play a role in hypertensive disease actively, passively, or incidentally. Much attention has been directed to the active participation of the heart in the development of hypertension. A number of workers have suggested a so-called cardiogenic role of the heart in the development of hypertensive disease, and while this concept is not directly applicable to the overall thesis of this symposium, it is fair to conclude that the role of a hyperdynamic circulation manifested by increased cardiac output and myocardial contractility has not been documented as a necessary pathogenetic factor in the elaboration of hypertensive heart disease. In general, most data support the thesis that increased cardiac output, heart rate, and myocardial contractility are most likely secondary to increased adrenergic drive to the heart. An autoregulatory phase with an increased cardiac output is not a required permissive phase for the later development of increased arterial pressure manifested by an increased total peripheral resistance.

Active Role

What may be interpreted as an active role of the heart, however, may be the elaboration from the heart of a humoral agent. In recent years a low molecular weight polypeptide substance has been isolated from hearts of experimental animals and humans that may have a pathogenetic role not only in hypertension but in other cardiac disorders. However, neither this factor nor the endogenous tissue levels of myocardial catecholamines, cardiogenic neural influences, or the interaction of humoral substances with the cardiac myocytes or neurones are relative to our present discussion.

Passive Role

What is more appropriate to this discussion is the role of the heart in response to hypertensive disease. Clearly, the adaptive left ventricular hypertrophy associated with the ever-increasing and progressive left ventricular afterload that characterizes hypertensive vascular disease is the first consideration in this regard. This adaptive hypertrophy is demonstrable echocardiographically as well as by other clinically useful diagnostic means. The increased left ventricular mass produced by hypertrophy in hypertension is associated with increased myocardial oxygen demand and myocardial fibrosis. Other cardiac alterations related to hypertensive heart disease are the cardiac dysrhythmias associated with ventricular hypertrophy or ischemia and the facilitated development of coronary atherosclerosis and its attendant increased morbidity and mortality.

Incidental Role

Receiving less attention over the years, but perhaps of more recent concern, are the incidental clinical cardiac conditions that are associated with hypertension, including the close association of exogenous obesity with hypertension. In recent years more attention has been directed to the physiologic relationships of these closely related two disorders. These studies have demonstrated that exogenous obesity per se is related to expanded intravascular volume, and when this cardiovascular risk is superimposed upon hypertensive heart disease a dual overload of volume and pressure is thrust upon the left
ventricle. Therefore, when obesity and hypertension coexist, there is an augmented cardiovascular risk that is greater than when either factor exists alone. These volume and pressure loads impose dual structural adaptive stimuli that promote both eccentric and concentric adaptive hypertrophy. Even though the problem of obesity heart disease remains incompletely understood at this time, it has been less well evaluated in patients with hypertension, in whom the problem is yet still more complex because of the frequent coexistence of hypertension and obesity with coronary atherosclerosis, diabetes mellitus, hyperuricemia, and other conditions.

Another area that has received a great deal of attention and is particularly of echocardiographic interest involves the recent experimental and clinical findings that the increased cardiac mass in hypertension may regress in size following treatment with certain antihypertensive agents. It is of particular interest that some agents that may exert more beneficial hemodynamic effects in controlling arterial pressure may not be associated with regression of cardiac mass, whereas other agents that perhaps have less salutary hemodynamic effects could produce significant regression of cardiac mass. In general, those classes of antihypertensive agents that have been shown to produce regression of left ventricular hypertrophy (i.e., cardiac mass) include drugs that inhibit the adrenergic nervous system, the angiotensin converting enzyme, and the slow entry channels for calcium ions. In contrast, the other vascular smooth muscle relaxants and centrally active α-adrenergic receptor agonists do not seem to have any effect on cardiac mass. These experimental findings in laboratory animals have been confirmed recently in humans.

Other changes associated with antihypertensive therapy have been related to electrolyte balance and cardiac rhythmicity, but clearly these have less relevance to echocardiographically oriented studies.

It might be well to point out that over and above these hemodynamic and pharmacologic factors that directly affect cardiac mass, a variety of other variables have also been incriminated in the elaboration of left ventricular hypertrophy including the age, race, and sex of the patient and some of the associated diseases referred to above. For this reason it would be wise for clinical investigators to consider the foregoing well in advance of planning any prospectively designed controlled study.

Echocardiographic Studies

Dunn and his colleagues were the first to apply echocardiographic techniques to clinical investigative studies of hypertensive patients. Until that time it was held that functional as well as structural assessment of the left ventricle might be invalid because of the possibility of ventricular dyskinesia associated with cardiac disease. In their report the authors excluded any patients having any possibility of clinically significant coronary artery disease, and they confirmed their previous physiologic studies concerned with hypertensive heart disease. These studies demonstrated that associated with increasing arterial pressure and total peripheral resistance (in patients with essential hypertension) was a progressive increase not only in left ventricular mass index but also in the thickness of the ventricular septum and free posterior wall of the left ventricle. Further, the echocardiographic measurements were performed in conjunction with indicator–dilution measurement of cardiac output and demonstrated that the simultaneous echocardiographically measured cardiac output values correlated well with the dye-curve measurements. These studies confirmed that those patients with hypertension having no evidence of cardiac abnormality (by chest roentgenogram or electrocardiogram) had a normal resting cardiac output and myocardial contractility and no evidence of cardiac enlargement by echocardiographic assessment. When electrocardiographically evident left atrial abnormality was present, however, left ventricular mass and wall thickness were significantly increased. In addition, these patients with electrocardiographic evidence of left atrial abnormality did, in fact, have echocardiographic evidence of left atrial enlargement. These cardiac structural changes that were predicted by electrocardiographic changes in the P wave preceded the more obvious clinical stages of left ventricular hypertrophy that were demonstrable by the conventional electrocardiographic criteria of left ventricular hypertrophy or by enlarged heart on chest roentgenogram. At this latter stage of enlargement, the echocardiographic measurements demonstrate that left ventricular mass has increased further. These studies gave impetus for use of the echocardiogram for assessing not only structural but also functional myocardial changes. More recent functional studies have been related to the diastolic function of the left ventricle in the early stage of hypertensive heart disease and how this may be adversely affected in the early stages of the development of hypertensive heart disease.

Other work from our laboratory employed echocardiographic techniques for demonstrating that in obesity-related hypertension the volume overload associated with obesity confounded the already pressure-overloaded hypertensive left ventricle. And those clinical studies that demonstrated regression of left ventricular hypertrophy with antihypertensive drug treatment (referred to above) have been accomplished using echocardiographic measurements.

Echocardiogram-Oriented Questions

Septal Hypertrophy

Certain early studies involving echocardiographic techniques reported that even before ventricular enlargement is demonstrable there may be an increase in size of the interventricular septum, although other reports have failed to confirm this finding. This question of whether septal hypertrophy exists in borderline hypertension must be resolved since inherent in the observation is the question of whether this represents a variant of asymmetric septal hypertrophy. Well known is the increased morbidity and mortality that is associated with this abnormality.

Mitrail Prolapse

Idiopathic mitral valve prolapse is a commonly found entity reported in a great percentage of the general population. In some patients this might be totally innocent and is observed echocardiographically in asymptomatic individuals. However, it may also have other clinical prognostic implications with therapeutic import. We have recently observed a number of patients with borderline hypertension who have evidence of an echocardiographically demonstrable mitral valve prolapse associated with other signs and symptoms of the idiopathic mitral valve prolapse syndrome. When these individuals were given an intravenous infusion of the β-adrenergic receptor agonist isoproterenol, the mitral valvular prolapse was made more evident on the electrocardiogram and the hemodynamic responses were aggravated as compared with individuals not having a prolapsed mitral valve. With treatment using a β-adrenergic receptor blocking drug, the prolapse may disappear, suggesting that increased endogenous adrenergic input to the myocardium may be fundamentally responsible for the mitral prolapse on the basis of enhanced ventricular contractility by pulling the posterior leaflet of the mitral
valve into the prolapse position. These observations have been confirmed but require further attention and study.\textsuperscript{38}

**Idiopathic Hypertrophic Subaortic Stenosis**

There have been intermittent reports in the cardiovascular literature of normotensive patients having a documented idiopathic hypertrophic subaortic stenosis who later developed hypertension.\textsuperscript{29, 60} This has led to the suggestion that idiopathic hypertrophic subaortic stenosis may be a preceding stage in the development of hypertensive heart disease. Echocardiographic studies would also help resolve this question.

**Definition of Left Ventricular Hypertrophy**

The medical literature depends on measurable criteria for the definition of abnormalities. And so it is with the criteria for the existence of left ventricular hypertrophy. These definitions are based on increased left ventricular mass and specific ventricular chamber dimensions. However, a word is in order about the necessity to develop more sophisticated means for defining the elaboration of ventricular hypertrophy. If, for example, the hemocrit of an individual that is usually 52% (the normal range is 40—48%) becomes reduced to 42%, would not the change be significant, even though a 42% hemocrit is well within the normal range? Similarly, if one of the left ventricular wall measurements using echocardiographic techniques demonstrates a consistent thickness of 0.6 cm, would not a definite increase in thickness to 1.0 cm be significant, even though the 1.0 cm thickness is generally accepted as being within the normal range? The point of this discussion, then, is to emphasize the importance of changes in left ventricular chamber dimensions in defining an hypertrophied ventricle; it should not simply rely upon established normal values for single measurements at one point in time.

**Epidemiologic Applicability**

It is well known that even in a normal population a significant percentage of echocardiographic measurements may be technically unacceptable for clinical as well as physiologic study. It is also well known that the confounding factor of obesity will further increase the number of technically unacceptable echo-cardiographic studies. As already indicated, it is similarly well known that obesity is found in a greater percentage of patients with hypertension than in the normal population. It therefore follows that echocardiographic measurements should not and do not lend themselves for meaningful epidemiologic studies. Many individuals would be excluded from the analysis of a defined population, thereby invalidating an epidemiologic study. Directions and concepts may be derived therefrom, but efforts to establish prevalence and incidence rates for population groups by using echocardiographic techniques would be fraught with inherent error.

**Functional and Structural Applicability**

Nevertheless, it follows that the echocardiogram should lend itself well for study and use in assessing the functional and structural alterations associated with the progression of hypertensive heart disease and the effects of antihypertensive therapy on its natural history. In order to prevent fallacious entrapment by our data, however, it is of the utmost necessity to establish criteria for technically acceptable echocardiographic recordings, means for identifying reproducible sequential measurements, and standards for more precise probe placement and angulation and other technical factors. We must develop means to ensure reproducible tracings and data. Notwithstanding these potential technical hazards, echocardiography will no doubt continue to emerge as a valuable clinical and physiologic tool for the assessment of patients with hypertension and for understanding the natural history of the disease.

**Experimental Studies**

There is one final factor: since echocardiographic techniques have already been applied by ophthalmologic investigators for assessment of lens dimensions, it should be feasible to refine our technology so that the echocardiogram may be used in experimental animals — even as small as the rat.

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